THE SYNTHESIS OF LARGE RING COMPOUNDS CONTAINING NITROGEN

BY

RICHARD CUNEO FOX

B. S., Massachusetts Institute of Technology, 1950

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ACKNOWLEDGMENT

The author wishes to express his sincere gratitude to Dr. Nelson J. Leonard for his advice, guidance and aid during the course of this research. He also wishes to thank the members of the senior staff for their kind help and suggestions, as well as Dr. E. J. Corey, Dr. H. Dryden and a host of graduate students whose aid both direct and indirect helped produce whatever might be significant in this research. He also wishes to thank the University of Illinois, the Sinclair Refining Company and the E. I. du Pont de Nemours and Company, Inc., for their financial assistance.

THE SYNTHESIS OF LARGE RING COMPOUNDS CONTAINING NITROGEN

INTRODUCTION

The purpose of this work was to prepare a series of large ring acyloins containing nitrogen as part of the ring. These compounds were to be studied for their ability to coordinate with various metal ions in a tridentate manner, with both oxygens and the nitrogen participating in bond formation. These new compounds were also to be studied qualitatively for comparison of their reactions with hydroxyl and carbonyl reagents, as well as for the ability of some of the derivatives (*e. g.* oximes) to form chelate complexes with the nitrogen group participating. There were indications that these acyloins might also possess some physiological activity.

DISCUSSION

The following ring compounds containing nitrogen were synthesized: 1-Phenyl-1-azacycloheptan-4-ol-5-one, 1-ethyl-1-azacyclononan-5-ol-6-one, 1-methyl-1-azacyclononan-5-ol-6-one, 1-ethyl-1-azacyclohendecan-6-ol-7-one, 1-methyl-1-azacyclohendecan-6-ol-7-one, 1-ethyl-1-azacyclotridecan-7-ol-8-one, 1-methyl-1-azacyclotridecan-7-ol-8-one, 1-ethyl-1-azacyclopentadecan-8-ol-9-one, 1-methyl-1-azacyclopentadecan-8-ol-9-one, 1-methyl-1-azacycloheptadecan-9-ol-10-one, 1-methyl-1-azacyclononadecan-10-ol-11-one, and 1-ethyl-1-azacyclotricosan-12-ol-13-one. Several attempts were made to synthesize 1-benzoyl-1-azacycloheptan-4-ol-5-one and 1-ethyl-1-azacycloheptan-4-ol-5-one, but were unsuccessful. The benzoyl case yielded extensive decomposition during the reaction and the ethyl compound proved to be unstable towards heat, with all attempted derivatives existing in an impure state. The rings were prepared by causing the appropriate diethyl ω,ω'-alkylimino-bis-alkyl esters to react with sodium in refluxing xylene or toluene as described for the acyloin condensation (1, 2). The yields for the rings larger than the seven-membered were good and seemed to depend on the isolation procedure rather than on the reaction. The yield of the one

seven-membered ring compound prepared was low in comparison with that for the rings of larger size. The aminodiesters were usually obtained by allowing the appropriate alkylamine to react with the respective ω-halogen esters (3). The infrared spectra and physical properties of the acyloins were determined. The reactions of the acyloins towards *p*-nitrobenzoyl chloride and hydroxylamine were also studied. There was a difference of chemical and physical properties in the nine-, eleven- and thirteen-membered ring region from the higher members or the straight chain analogs. These intermediate acyloins appeared to form unstable *p*-nitrobenzoates, and treatment with excess hydroxylamine hydrochloride and pyridine in refluxing ethanol resulted in a dioxime instead of a monoxime. The infrared maximum for the carbonyl stretching was shifted to lower frequencies.

The complexing abilities of the N-methyl acyloins towards cobaltous, cupric, chromic, ferric and nickel ions were qualitatively assessed by mixing solutions of the various acyloins with solutions of the metal ions and observing any unusual changes of color or precipitation. These tests were run in both ethanol and water solutions and under acidic, basic and neutral conditions. Only the N-methyl nine-membered ring showed any tendency to complex. Unfortunately, a more thorough study of the complexes of this compound was complicated by the fact that the complexes did not seem to be very stable.

The N-methyl acyloins were converted to their respective dioximes by oxidation and reaction with hydroxylamine. The dioximes were qualitatively studied with respect to cobaltous, cupric, chromic, ferric and nickel ions under the same conditions mentioned above. In general, these dioximes showed the same reactions as did dimethylglyoxime except that the nickel salts were very water soluble and the N-methyl nine-membered ring did not form a stable nickel salt.

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VITA

The author was born in San Francisco, California, on November 4, 1927, and there he received his elementary education. He was graduated from St. Ignatius High School, San Francisco, California, in 1945. He entered the Massachusetts Institute of Technology in July, 1945. From 1946 to 1948 he served in the United States Army. He finished his studies at the Massachusetts Institute of Technology in 1950, receiving the Bachelor of Science Degree. He entered the University of Illinois in 1950. He held a University assistantship 1950-1951, a Sinclair Fellowship 1951-1952, and a duPont Fellowship 1952-1953.